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THE TOXINE OF SYPHILIS.

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TODAY we will call your attention to the toxine of syphilis. It is generally admitted that the virus of syphilis depends upon an organism, and that after it has gained entrance into the body, it increases indefinitely. The cutting out or destroying the point of inoculation does not prevent the spread of the disease. It has been absorbed by the lymphatics and then through the blood is distributed to every tissue of the body. As in other diseases caused by bacteria, such as septicemia, certain symptoms occur, showing that the entire system is poisoned. This poison is the product of bacteria.

Dr. Green, in his book on "Pathology and Morbid Anatomy, 1895," writes: "Albumoses are common intermediate products in the sequence of bacterial reactions. In some cases they are the most virulent of all the resulting compounds. This is so in diphtheria and in snake poison. In anthrax and cholera, on the other hand, they are comparatively of slight importance. Among the varied products of bacterial growth are a large number of alkaloid substances; some of these are harmless, but some are poisonous. The latter are known as toxines. Examples of both these varieties may be found in putrefying meat, fish and cheese. They can be easily separated and their nature investigated. The virulence of both anthrax and cholera is due to the formation of toxines."

The toxine of syphilis varies in virulence according to the soil in which it is implanted. Some have the disease so mildly as to recover without treatment. Others having acquired the disease from the same source, are poisoned in the most malignant manner, and go from bad to worse, in spite of the most approved treatment.

The diagnosis of syphilis having been made, the patient can be assured that the long continued and intermittent administration of drugs will prevent the formation, or destroy and eliminate from the system the toxine or poison of syphilis.

There is no antitoxine for the syphilitic poison. The man who indulges his licentious passions and breaks the Seventh Commandment must take the risks. The disciples of Auzias Turenne thought that "syphilization" would do for the great- what vaccination did for the smallpox. That it would make them immune. I have told you that their hopes were blasted. So it will be with the antitoxine treatment, for the reason that all animals are already immune, rendering it impossible to procure the antitoxine through them. Very numerous efforts have been made to impart syphilis to the brute creation.

Dr. Rebatel, in the *Lyons Medical Journal*, January 8, 1882, gives an interesting account of how he recently had been making a series of experiments on animals, with a view to test anew the question, whether or not they are susceptible to any of the several venereal diseases of mankind. His subjects were dogs, rabbits and guinea-pigs. No trace of consecutive inflammation was ever seen. Another series of experiments was performed with material from a soft chancre; the results were negative, as in the former case. Finally he took two hard chancres, that had been removed in the operation of circumcision; then making slits in the inguinal folds of a bitch, he inserted them, sewing up the openings. No symptoms of infection followed. Into the jugular vein of a dog, he next injected one hundred and fifty grammes of defibrinated blood, taken from a patient in the full

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tide of secondary syphilis. No ill-symptoms followed, but in due course of time these two animals contributed mutually to the production of a litter of puppies, twelve in number. Nor did these young manifest any congenital disease, or in fact anything but the most exuberant health.

In 1883, my friend and former professor, Dr. Isidor Neumann of Vienna, made a number of attempts to inoculate animals with syphilis, but without success. In no case did any results follow other than those which would naturally appear on introduction of an irritating material into the tissues. Neumann concluded from these experiments that we must regard syphilis as distinctly a disease of man.

These experiments were made on animals long before the antitoxine treatment was thought of. We knew that measles, or scarlet fever, or smallpox, as a rule, occurred but once.

Edward Jenner was the first to carry out the idea of making human beings immune from the smallpox by means of vaccination. Pasteur was the first to experiment on animals resulting in the discovery of the antitoxine for hydrophobia. You will say, as animals are immune to syphilis, then their serum is already antitoxine to the poison of syphilis. Why not use that? It has been tried. I will relate the experiments of various syphilographers, as reported by Mueller-Kannberg in the *Archives for Dermatologie and Syphilologie*, 1896.

Kollman, in 1890, was the first to make use of the serum of animals in syphilis. In 1892 Tommasoli recorded a brilliant success in six cases of recent syphilis, treated by the injection of lamb's serum. Hericourt and Richet have recorded favorable results, while others have been totally unsuccessful.

Experiments were made on twelve patients at Lewins' clinic in the Charité at Berlin, and the results are described in Mueller-Kannberg's paper. The serum was obtained from horses, a source that had never before been made use of in syphilis. As a preliminary trial two patients were given an injection of

five cubic centimeters of the serum. Their general condition remained unaltered, but five days later each experienced an attack of urticaria which lasted seventeen days. Another patient treated in the same way developed such grave symptoms that no further trial was made. In the remaining cases no positive influence on the syphilitic process could be claimed. Urticaria was almost universally produced, sometimes of an exceedingly annoying and obstinate type. Some of the patients received at intervals as much as five injections without effect upon the disease. The writer remarks, in conclusion, that no encouraging deduction can be drawn from these experiments, which are the same as those of Kollman. The urine in these cases remained normal.

Professor Neumann of Vienna has recently been carrying on a series of investigations on the treatment of syphilis by the serum of animals immune to this affection, but with results far from being satisfactory. The ordinary methods still show the best results. He pleads that the number of his cases was too few to condemn the method, especially as other "syphilographers" have met with some success; therefore, he would recommend a continuance of the experiments.

In the *Archives für Dermatologie und Syphilologie*, Professor Tornowski of St. Petersburg related his experiments with the serum treatment of syphilis, and is reported as follows: "Reflecting upon the absence of positive results from employing the normal serum of animals, that of animals inoculated with syphilitic products, or that of persons affected with constitutional syphilis, Tornowski thought it most rational to use serum obtained by a process as nearly as possible the same as the one employed in the preparation of anti-diphtheritic serum; but the practical difficulty presented itself of finding an animal susceptible to syphilis. However, he thinks he has found such an animal in the foal. Although, on inoculation, the foal does not show any outward signs of syphilis, changes extraordinarily like those due to that disease are found in different in-

ternal organs, and in the blood-vessels and the lymphatic glands in the course of two or three months. Accordingly, he has endeavored to syphilize two foals with moist syphilitic papules by implanting them in incisions into the skin, by applying them to a blistered surface, and by injecting an emulsion of them subcutaneously. After these inoculations had been many times repeated, blood was drawn from the animals, and the serum was administered subcutaneously to six patients, usually in doses of from ten to twenty cubic centimeters. In five of the patients the disease was quite recent and had not been treated before; the remaining one had tertiary manifestations. The therapeutic result was nil, even after long persistence in treatment; the cases followed their course precisely as if no treatment had been practiced. Moreover, the injections seemed to have had a detrimental effect. Three of the patients lost flesh, their general health grew worse and they had transitory albuminuria. In four cases an itching erythema appeared, with pains in the muscles and joints, also purpura in two instances. When large doses were used the temperature was decidedly raised."

Gilbert and Fournier (*Sémaine Médicale*, April 27, 1895) inserted under the skin of certain animals the serum of the blood, chancres and papules obtained from patients suffering from primary and secondary syphilis, with the object of increasing the natural antagonism of the blood of these animals to the syphilitic poison.

The patients treated by the serum obtained from the animals thus prepared were seventeen in number. Of these, seven underwent the usual anti-syphilitic treatment concurrently with the serum injections. All improved; but the authors hesitate to ascribe much force to these cases. The results on the other ten cases were contradictory. While some of them showed marked improvement under the treatment, others appeared to be uninfluenced by it. A patient may be instanced who presented at the commencement of the treatment three cicatrized preputial chancres,

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roseola confluens and headaches, worse at night. In the space of twenty days he received forty-eight cubic centimeters of serum in seven injections. The roseola paled, but nevertheless persisted; hence, although the man's other symptoms and general condition were favorably influenced, the authors are inclined to regard the results as negative. Farther researches are in progress.

You will say that the so-called tertiary stage is the product of bacteria. It is the toxine of syphilis. The cases of reinfection are so uncommon that the victims of syphilis are considered to be immune against another attack of the disease. Why not take the serum from one already suffering from tertiary syphilis! This has been done, and experiments are still being made. Gilbert and Fournier, adopting the method of Pellizzari, took the serum obtained from the blood of a patient with a clear history of old syphilis and suffering from tabes, but in a very satisfactory general condition, and from another patient who had had gummata and was under treatment for obstruction of the vena cava superior. The subject of the experiment was a patient until then untreated, having two infecting chancres on the penis, double buboes, anemia, headache at night, aching in the joints and bones and a general maculo-papular eruption, most intense on the trunk. He received three hundred and four cubic centimeters of serum in twenty days, the average dose being 35 cubic centimeters. During that time the chancres cicatrized, his pains vanished, the general condition was much ameliorated and the eruption disappeared, except a slight lingering roseola. The eruption was earliest influenced and soonest gone on the front of the abdomen at about the level at which the injections were made. This local action was very striking.

Cotterell (*Medical Press and Circular*, August 28, 1895) states that he has treated eighteen cases of syphilis by injection of the serum of blood of patients who had gone through an attack of syphilis and were rendered immune. He does not state the age of the disease, nor of the patient or patients from whom

he obtained the serum, nor are any details given. The treatment was pursued over six months. The conclusions are as follows, viz: In the early stages of syphilis, *i. e.*, when there is only a sore and glandular enlargement, injections of this serum cause the sore to heal rapidly. The adenitis in the groin generally becomes intensely marked; the skin and throat symptoms are absent or only slightly marked. When the case is not seen until the rash and throat symptoms develop, the skin eruption fades rapidly, much more rapidly, as a rule, than under mercurial treatment, but the throat symptoms disappear rather slowly. The general health improves. The serum from an individual with well marked secondary syphilis appears to be more active than that obtained from a patient with tertiary symptoms. The author has not yet accurately determined the amount to be injected, but he has used the serum in doses from $\frac{1}{2}$ to 5 cubic centimeters.

Boeck, since November of 1894 (*Archiv für Dermatologie und Syphilologie*, July 3, 1896), has treated seven patients by injections of the hydrocele fluid drawn from a man in the sixth year of syphilis. This fluid was filtered before being injected. He was astonished at the results. The first case received in all $6\frac{1}{2}$ drachms of the serum. Eight days before the time the secondaries should have developed, the injections were begun, a drachm being employed every second day. The large chancres and the marked swelling of the glands disappeared promptly. Although the exanthema appeared after the regular time, it was very slight and lasted only a few weeks. There were no mucous patches. The second case was given serum injection sixty days after infection; from fifteen to sixty minims were employed at a time; in two months all secondary symptoms had disappeared. Similar improvement was noted in all the cases. He holds that the effect of this treatment is observed in the quick disappearance of the primary symptom, the abortion or marked amelioration of all secondary symptoms and the improvement in general condition. The

treatment is potent in proportion to the promptness with which the injections are begun. The serum treatment is not as prompt and evident in its effects as iodides and mercury, but it is more rational.

Tonimasoli (*New York Medical Journal*, September 26, 1896) took the ascitic fluid of a person affected with syphilitic disease of the liver. This he employed upon seven patients in the tertiary stage, most of whom had had no previous specific treatment. The smallest number of injections given in any one case was eight and the largest thirty-seven, in periods ranging from ten to fifty-seven days, and the total amount injected varied from 68 to 350 cubic centimeters. The fluid was obtained with all antiseptic precautions and used either fresh or after being kept in sterilized vessels with the addition of a few drops of chloroform; it was injected into the buttocks and no serious mishaps occurred in any case. In most patients, soon after the injection, there followed indisposition, headache, giddiness, etc., but these disturbances always subsided speedily. No albumen was ever found in the urine. As to the effect on the disease, all that can be said with certainty is that new symptoms made their appearance during the course of injections.

Tommasoli also used the milk of two women who had secondary syphilis—latent in one of them. After proper cleansing of the nipples the milk was pressed out and injected immediately into the muscles of the buttock. Of seven patients treated by this method, one had gummatous syphilis, but all the others were in the secondary stage. The number of injections varied from three to thirteen; and the total amount injected into any one patient ranged from 30 to 100 cubic centimeters. Ten of the patients in the secondary stage were decidedly improved; the others showed no change. This method was based on the observation that in other infectious diseases, such as tetanus and diphtheria, the antitoxines pass into the milk.

The result of these experiments show

that tertiary products, such as fluids obtained from a syphilitic hydrocele and ascitic fluid result of syphilitic liver disease when injected into the tissues of the body, have a curative action upon constitutional syphilis. Cotterell goes farther and says: "The serum from an individual with well marked secondary syphilis appears to be more active than that obtained from a patient with tertiary symptoms."

Suppose we take it for granted that we have an antagonistic virus and some young man comes along and wants to be "immunized" against syphilis. If we were to inject a tertiary product, per-

haps it would do no harm. Should we take the serum, or blood, or pus from a mucous patch, we would have as a result a chancre at the point inoculated. Galligo of Florence experimented on himself, taking the pus from a mucous patch. The result was a chancre which developed seventeen days after, followed by roseola, etc. Likewise, where syphilitic blood was inoculated, as in the case of Dr. Bargioni, who voluntarily submitted to be experimented upon with the blood of a syphilitic woman.

No Jenner has appeared with his magic wand to do with the great- what that great man did for the small-pox.

